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| EXAMINER | |
|---|---|
| BROOKS, KRISTIE LATRICE | |
| ART UNIT | PAPER NUMBER |
| 1609 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/519,008 | BELANOFF, JOSEPH K. | |
| | Examiner | Art Unit | |
| | Kristie L. Brooks | 1609 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *5-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 8-22* is/are rejected.

7)☒ Claim(s) *8 and 12* is/are objected to.

8)☒ Claim(s) *4-7* are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. This application contains claims directed to the following patentably distinct species: glucocorticoid receptor antagonists. The species are independent or distinct because the species consist of both steroidal and non-steroidal glucocorticoid receptor antagonist where different biological activity or selective receptor binding activity can result from different chemical and physical properties of each species. Therefore election of species requirement for examination purposes as indicated is proper.

**Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for a glucocorticoid receptor antagonist for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 4-7 are generic.**

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

### *Telephone Election*

2. During a telephone conversation with Attorney Kenneth A. Weber on April 25, 2007 a provisional election was made with traverse to prosecute the invention with elected glucocorticoid receptor antagonist mifepristone of claim 4. Affirmation of this election must be made by applicant in replying to this Office action. Claims 5-7 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

### *Status of Application*

3. Claims 1-22 are pending.

4. Election of species of glucocorticoid receptor antagonist, mifepristone in claim 4 is acknowledged (see page 3, telephone election).

5. The elected claims 1-4 and 8-22 are presented for examination and the non -elected claims 5-7 are withdrawn from consideration.

### *Specification*

6. The abstract of the disclosure is objected to because it is not descriptive enough of the invention. The abstract should be between 50-150 words in length. Correction is required. See MPEP § 608.01(b).

### *Claim Objections*

7. Claim 8 is objected to because of the following informalities: a period is missing at the end of the claim.

Appropriate correction is required.

8. Claim 12 is objected to because of the following informalities: a typographical error in the spelling of "ribavarin" should be corrected to -- ribavirin--.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 102*

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-4, 13-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Schatzberg et al. (US 6,150, 349).

The claims are drawn to a method of ameliorating the symptoms of psychosis associated with interferon-α therapy in a patient comprising administering an amount of a glucocorticoid receptor antagonist effective to ameliorate the symptoms of psychosis in the patient, with the proviso that the patient is not otherwise in need of treatment with a glucocorticoid receptor antagonist.

Schatzberg et al. teaches a method of ameliorating psychosis associated with glucocorticoid related dysfunction by administering an effective amount of a glucocorticoid receptor antagonist, where the glucocorticoid receptor antagonist used in the methods can comprise a steroidal skeleton with at least one phenyl-containing moiety in the 11-beta position of the steroidal skeleton where the phenyl-containing moiety in the 11-beta position of the steroidal skeleton can be a dimethylaminophenyl moiety and the glucocorticoid receptor antagonist can comprise mifepristone (RU486), 11-β-(4-dimethyl-aminoethoxyphenyl)-17α-propynyl- 17β-hydroxy-4,9-estradien-3-one(RU009), and 17β-hydrox-17α -19-(4-methyl-phenyl)androsta-4,9 (11)-dien-3-one (RU044) (see the entire article, especially column 3 lines 46-63; column 10 lines 7-21). The glucocorticoid antagonist can be administered by oral administration, topical administration, aerosol formulations, where the dosage of mifepristone can be about 2-30mg per kg of body weight per day (see the entire article, especially column 20 lines 25-45; column 21 lines 56-68).

13. Claims 20-22 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Rubinfeld (US Pub No. 2002/0111362).

The claims are drawn a kit comprising (i) interferon-or, (ii) a specific glucocorticoid receptor antagonist and, (iii) an instructional material teaching the indications, dosage and schedule of administration of the glucocorticoid receptor antagonist and interferon-α to a patient suffering from hepatitis C infection.

Rubinfeld (US Pub No. 2002/0111362) teaches a kit comprising: a container that contains a compound selected from the group consisting of 20(S)-camptothecin, analog of 20(S)-camptothecin, derivative of 20(S)-camptothecin, prodrug of 20(S)-camptothecin, and pharmaceutically active metabolite of 20(S)-camptothecin, and one or more agents selected from the group consisting of alkylating agent, antibiotic agent, an alkylating agent, antibiotic agent, antimetabolic agent, hormonal agent (e.g. mifepristone), plant-derived agent, anti-angiogenesis agent and biologic agent where the biological agent is selected from a group consisting of immuno-modulating protein (e.g. interferon-α), monoclonal antibody against tumor antigen, tumor suppressor gene, and cancer vaccine (see the entire article, especially the abstract; page 4 paragraph [0041], [0043]- [0044]; page 7 paragraph [0071]; page 9 paragraph [0090]; and claims 1,5-7, and 26-28).

It is noted that that Rubinfeld does not explicitly teach a kit containing instructional material teaching the indications, dosage and schedule of administration of

the glucocorticoid receptor antagonist and interferon-α to a patient suffering from hepatitis C infection. However, where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art and thus will not have any patentable weight. See MPEP 2112.01.

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 1-4, 8-12, and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korant (US 6,649,644) in view of Bozikas et al. *(A interferon-α-*

*induced psychotic disorder in a patient with chronic hepatitis C*, European Psychiatry, vol. 16, pages 136-137, 2001).

The claims are drawn to a method of ameliorating the symptoms of psychosis associated with interferon-α therapy in a patient comprising administering an amount of a glucocorticoid receptor antagonist effective to ameliorate the symptoms of psychosis in the patient, with the proviso that the patient is not otherwise in need of treatment with a glucocorticoid receptor antagonist.

Korant teaches a method of treating chronic viral infections, such as hepatitis B virus and hepatitis C virus comprising administering to a mammal a therapeutically effective amount of a combination (i.e. concurrently, sequentially or at the same time) of: (i) at least one cytotoxic agent (e.g. cyproterone acetate (which is also a glucocorticoid receptor antagonist)) and (ii) at least one antiviral agent such as interferon alpha, and interferon alpha plus virazole (also known as ribavirin) (see the entire article, especially the abstract; column 2 lines 59-67; column 3 lines 25-33 and lines 63-67; column 4 lines 1-13, lines 30-40 and lines 44-48)

Korant does not expressly teach ameliorating the symptoms of psychosis associated with interferon-α therapy.

Bozikas et al. teaches a case of induced INF-α2b psychotic symptoms in a man with chronic hepatitis C one day after the administration of his standard dose of INF-α2b (see the entire articles, especially the first and second paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to ameliorate the symptoms of psychosis associated with interferon-α therapy comprising administering a glucocorticoid receptor antagonist, interferon- α and ribavirin. One of ordinary skill in the art would have been motivated to do this because Korant suggests the combination of a cytotoxic agent such as cyproterone acetate (i.e. a glucocorticoid receptor antagonist) and at least one antiviral agent such as interferon alpha plus virazole (also known as ribavirin) in the treatment of viral infections such as both hepatitis B and hepatitis C. It is well known in the art that neuropsychiatric side effects, including psychosis, are associated with interferon-α treatments in patients with chronic hepatitis C as suggested by Bozikas et al. and it would be obvious to ameliorating the symptoms of psychosis as claimed in the instant invention because the method taught by Bozikas et al. is composed of the same ingredients.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

***Conclusion***

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:00am-5:30pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KB

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SUPERVISORY PATENT EXAMINER